Supporting Information

Electrophilic Behavior of the π Delocalized Azepinium ion: Friedel-Crafts Reactions with Benzenes and Five-membered Aromatic Heterocycles

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1. General information

^1H and ^{13}C NMR spectra were recorded on a Varian XL-200, Varian Mercury 300, Varian VXR-500 or Varian Unity Inova AS600 spectrometer. Infrared spectra were recorded on a JASCO FT-IR 5000 spectrophotometer. Fast Atom Bombardment (FAB) mass spectra were recorded on a Micromass 70-SE. High Resolution Mass Spectra (HRMS) were obtained from the above instruments. Elemental analyses performed on a PERKIN ELMER CHNS/O Analyzer 2400. Melting Points were measured on a Yanagimoto micromelting point apparatus and are uncorrected. UV-Visible absorption was recorded on a Hitachi 288 spectrophotometer. Thin-layer chromatography (TLC) was performed on Silica gels HF₂₅₄ (Merck). The molecular orbital calculations were carried out on a NEC SX5 computer system of Okayama University Computer Center.

2. Experimental

Reaction of azepinium ion **2** with benzene

A solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**) (100 mg, 0.478 mmol) in absolute chloroform (30 mL) was treated with 3.8 molar amounts of TiCl_4 (0.2 mL, 1.8 mmol) at room temperature. After stirring for 1 min at room temperature, dry benzene (2.5 mL, 28 mmol) was

added. After stirring for 60 min at room temperature, aqueous NaHCO₃ (160 mg, 1.91 mmol) was added, after which extracted with chloroform. The extract was dried over MgSO₄ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 9 : 1) gave 4-*tert*-butyl-7-methoxy-2-phenyl-2*H*-azepine (**5**) (60 mg, Y = 49%) as a colorless oil and 5-*tert*-butyl-2-methoxy-3-phenyl-3*H*-azepine (**6**) (6 mg, Y = 5%) as a colorless oil.

4-*tert*-butyl-7-methoxy-2-phenyl-2*H*-azepine (**5**)

¹H NMR (500 MHz, CDCl₃) δ 1.13 (s, 9H), 3.79 (s, 3H), 4.15 (d, *J* = 5.5 Hz, 1H), 5.69 (d, *J* = 5.5 Hz, 1H), 6.59 (d, *J* = 12.0 Hz, 1H), 7.05 (d, *J* = 12.0 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.64 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 29.8 (q), 34.7 (s), 53.5 (q), 58.4 (d), 124.8 (d), 126.6 (d), 126.8 (d), 128.3 (d), 130.1 (d), 138.9 (d), 145.1 (s), 147.4 (s), 161.3 (s); IR (neat) 2968, 1636, 1441, 1241, 1203, 1007, 754, 700 cm⁻¹; UV-vis (EtOH) λ_{max} 287 nm (log ε = 3.44); MS (FAB) *m/z* 256 [M + H]⁺; HRMS (FAB) *m/z* calcd for C₁₇H₂₂NO [M + H]⁺ 256.1701, found 256.1675; Found: C, 79.83; H, 8.48; N, 5.28%. Calcd for C₁₇H₂₁NO: C, 79.96; H, 8.29; N, 5.49%.

5-*tert*-butyl-2-methoxy-3-phenyl-3*H*-azepine (**6**)

¹H NMR (500 MHz, CDCl₃) δ 1.14 (s, 9H), 3.09 (brs, 1H), 3.69 (s, 3H), 5.38 (d, *J* = 6.5 Hz, 1H), 6.24 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 7.29- 7.38 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 30.2 (q), 34.8 (s), 49.2 (d), 55.2 (q), 115.2 (d), 115.4 (d), 126.8 (d), 128.0 (d), 129.1 (d), 136.6 (d), 138.0 (s), 147.4 (s), 153.4 (s); IR (neat) 2966, 1620, 1319, 1278, 1249, 1013, 756, 700 cm⁻¹; UV-vis (EtOH) λ_{max} 255 nm (log ε = 3.69); MS (FAB) *m/z* 256 [M + H]⁺; HRMS (FAB) *m/z* calcd for C₁₇H₂₂NO [M + H]⁺ 256.1701, found 256.1708; Found: C, 80.24; H, 8.05; N, 5.61%. Calcd for C₁₇H₂₁NO: C, 79.96; H, 8.29; N, 5.49%.

Reaction of azepinium ion **2** with anisole

TiCl₄ (0.4 mL, 3.6 mmol) was added to a solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**)

(200 mg, 0.956 mmol) in absolute chloroform (50 mL) at room temperature. After stirring for 5 min at room temperature, anisole (1.0 mL, 9.3 mmol) was added. After stirring for 60 min at room temperature, aqueous NaHCO₃ (320 mg, 3.82 mmol) was added, after which extracted with chloroform. The extract was dried over MgSO₄ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 19 : 1) gave 4-*tert*-butyl-7-methoxy-2-(4-methoxyphenyl)-2*H*-azepine (**7a**) (128 mg, Y = 47%) as colorless prisms, 4-*tert*-butyl-7-methoxy-2-(2-methoxyphenyl)-2*H*-azepine (**7b**) (77 mg, Y = 28%) as colorless prisms, and 5-*tert*-butyl-2-methoxy-3-(4-methoxyphenyl)-3*H*-azepine (**8**) (9 mg, Y = 3%) as a colorless oil.

4-*tert*-butyl-7-methoxy-2-(4-methoxyphenyl)-2*H*-azepine (7a**)**

mp 73.5-74.5 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.14 (s, 9H), 3.79 (s, 3H), 3.84 (s, 3H), 4.12 (d, *J* = 5.5 Hz, 1H), 5.69 (d, *J* = 5.5 Hz, 1H), 6.60 (d, *J* = 12.2 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 7.05 (d, *J* = 12.2 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 29.7 (q), 34.6 (s), 53.4 (q), 55.2 (q), 58.0 (d), 113.6 (d), 124.7 (d), 127.8 (d), 130.4 (d), 137.3 (s), 138.7 (d), 147.1 (s), 158.3 (s), 161.2 (s); IR (KBr) 2958, 1634, 1512, 1444, 1238, 1210, 1035, 859, 826, 810, 576 cm⁻¹; UV-vis (EtOH) λ_{max} 278 nm (log ε = 3.58); MS (FAB) *m/z* 286 [M + H]⁺; HRMS (FAB) *m/z* calcd for C₁₈H₂₄NO₂ [M + H]⁺ 286.1807, found 286.1787; Found: C, 75.95; H, 8.02; N, 5.13%. Calcd for C₁₈H₂₃NO₂: C, 75.76; H, 8.12; N, 4.91%.

4-*tert*-butyl-7-methoxy-2-(2-methoxyphenyl)-2*H*-azepine (7b**)**

mp 67.0-68.5 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.11 (s, 9H), 3.77 (s, 3H), 3.78 (s, 3H), 4.42 (d, *J* = 5.4 Hz, 1H), 5.55 (d, *J* = 5.4 Hz, 1H), 6.54 (d, *J* = 12.0 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 12.0 Hz, 1H), 7.06 (dd, *J* = 8.1, 8.1 Hz, 1H), 7.27 (dd, *J* = 8.1, 8.1 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 29.9 (q), 34.7 (s), 53.5 (d), 53.6 (q), 55.4 (q), 110.3 (d), 120.5 (d), 123.8 (d), 127.4 (d), 128.0 (d), 131.0 (d), 133.3 (s), 138.9 (d), 146.2 (s), 156.7 (s), 161.1 (s); IR (KBr) 2968, 1638, 1491, 1464, 1439, 1234, 1203, 1031, 754 cm⁻¹; UV-vis (EtOH) λ_{max} 278 nm

(log ϵ = 3.83); MS (FAB) m/z 286 $[M + H]^+$; HRMS (FAB) m/z calcd for $C_{18}H_{24}NO_2$ $[M + H]^+$ 286.1807, found 286.1792; Found: C, 75.95; H, 8.25; N, 4.83%. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91%.

5-*tert*-butyl-2-methoxy-3-(4-methoxyphenyl)-3*H*-azepine (8)

1H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 9H), 3.10 (brs, 1H), 3.69 (s, 3H), 3.83 (s, 3H), 5.32 (d, J = 6.3 Hz, 1H), 6.23 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 8.9 Hz, 2H), 7.01 (d, J = 8.4 Hz, 1H), 7.24 (d, J = 8.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.2 (q), 34.8 (s), 48.4 (d), 55.2 (q), 55.3 (q), 113.5 (d), 115.2 (d), 115.7 (d), 124.4 (s), 130.1 (d), 136.5 (d), 147.2 (s), 153.6 (s), 158.4 (s); IR (neat) 2958, 1615, 1516, 1249, 824 cm^{-1} ; UV-vis (EtOH) λ_{max} 226 nm (log ϵ = 4.16), 256 nm (log ϵ = 3.71); MS (FAB) m/z 286 $[M + H]^+$; HRMS (FAB) m/z calcd for $C_{18}H_{24}NO_2$ $[M + H]^+$ 286.1807, found 286.1794; Found: C, 75.93; H, 8.00; N, 5.18%. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91%.

Reaction of azepinium ion 2 with phenol

$TiCl_4$ (1.0 mL, 9.1 mmol) was added to a solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**) (500 mg, 2.39 mmol) in absolute chloroform (60 mL) at room temperature. After stirring for 5 min at room temperature, a solution of phenol (2.25 mg, 23.9 mmol) in $CHCl_3$ was added. After stirring for 60 min at room temperature, aqueous $NaHCO_3$ (800 mg, 9.55 mmol) was added, after which extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 19 : 1) gave 4-*tert*-butyl-2-(4-hydroxyphenyl)-7-methoxy-2*H*-azepine (**9a**) (217 mg, Y = 33%) as a colorless oil, 4-*tert*-butyl-2-(2-hydroxyphenyl)-7-methoxy-2*H*-azepine (**9b**) (195 mg, Y = 30%) as a colorless prisms, and 5-*tert*-butyl-3-(4-hydroxyphenyl)-2-methoxy-3*H*-azepine (**10**) (18 mg, Y = 3%) as a colorless oil.

4-*tert*-butyl-2-(4-hydroxyphenyl)-7-methoxy-2*H*-azepine (9a)

^1H NMR (300 MHz, CDCl_3) δ 1.12 (s, 9H), 3.77 (s, 3H), 4.07 (d, $J = 5.4$ Hz, 1H), 5.05 (brs, 1H), 5.67 (d, $J = 5.4$ Hz, 1H), 6.57 (d, $J = 11.7$ Hz, 1H), 6.84 (d, $J = 8.6$ Hz, 2H), 7.03 (d, $J = 11.7$ Hz, 1H), 7.47 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 29.8 (q), 34.7 (s), 53.7 (q), 58.1 (d), 115.1 (d), 124.6 (d), 128.0 (d), 130.3 (d), 136.9 (s), 138.9 (d), 147.2 (s), 154.2 (s), 161.4 (s); IR (neat) 3350, 2966, 1636, 1613, 1516, 1441, 1241, 1205, 750 cm^{-1} ; UV-vis (EtOH) λ_{max} 285 nm ($\log \epsilon = 3.64$); MS (FAB) m/z 272 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{17}\text{H}_{22}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 272.1651, found 272.1666; Found: C, 75.01; H, 7.76; N, 5.11%. Calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_2$: C, 75.25; H, 7.80; N, 5.16%.

4-*tert*-butyl-2-(2-hydroxyphenyl)-7-methoxy-2*H*-azepine (9b)

mp 79.5-80.5 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 1.11 (s, 9H), 3.74 (s, 3H), 4.31 (d, $J = 5.7$ Hz, 1H), 5.71 (dd, $J = 5.7, 1.0$ Hz, 1H), 6.57 (d, $J = 11.8$ Hz, 1H), 6.83 (dd, $J = 7.5, 7.5$ Hz, 1H), 6.91 (d, $J = 7.5$ Hz, 1H), 6.94 (d, $J = 7.5$ Hz, 1H), 7.13 (dd, $J = 11.8, 1.0$ Hz, 1H), 7.19 (dd, $J = 7.5, 7.5$ Hz, 1H), 11.4 (s, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 29.7 (q), 34.8 (s), 54.4 (q), 60.0 (d), 117.6 (d), 119.3 (d), 123.3 (d), 126.0 (s), 128.3 (d), 128.4 (d), 130.6 (d), 130.6 (d), 140.5 (d), 147.6 (s), 157.1 (s), 162.6 (s); IR (neat) 3100, 2968, 1638, 1618, 1265, 754 cm^{-1} ; UV-vis (EtOH) λ_{max} 277 nm ($\log \epsilon = 3.33$); MS (FAB) m/z 272 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{17}\text{H}_{22}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 272.1651, found 272.1626; Found: C, 75.09; H, 7.60; N, 5.26%. Calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_2$: C, 75.25; H, 7.80; N, 5.16%.

5-*tert*-butyl-3-(4-hydroxyphenyl)-2-methoxy-3*H*-azepine (10)

^1H NMR (300 MHz, CDCl_3) δ 1.14 (s, 9H), 3.10 (brs, 1H), 3.69 (s, 3H), 5.10 (brs, 1H), 5.31 (d, $J = 6.3$ Hz, 1H), 6.22 (d, $J = 8.7$ Hz, 1H), 6.83 (d, $J = 8.6$ Hz, 2H), 7.00 (d, $J = 8.7$ Hz, 1H), 7.18 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.2 (q), 34.8 (s), 48.4 (d), 55.3 (q), 115.0 (d), 115.3 (d), 115.7 (d), 130.1 (s), 130.3 (d), 136.5 (d), 147.2 (s), 153.8 (s), 154.5 (s); IR (neat) 3300, 2966, 1615, 1601, 1518, 1323, 1280, 1251, 1011, 820 cm^{-1} ; UV-vis (EtOH) λ_{max} 226 nm ($\log \epsilon = 4.06$), 258 nm ($\log \epsilon = 3.67$); MS (FAB) m/z 272 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for

$C_{17}H_{22}NO_2$ $[M + H]^+$ 272.1651, found 272.1662; Found: C, 75.30; H, 8.06; N, 4.95%. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16%.

Reaction of azepinium ion **2** with thiophene

A solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**) (100 mg, 0.478 mmol) in absolute chloroform (30 mL) was treated with 3.8 molar amounts of $TiCl_4$ (0.2 mL, 1.8 mmol) at room temperature. After stirring for 1 min at room temperature, dry thiophene (2.5 mL, 31 mmol) was added. After stirring for 60 min at room temperature, aqueous $NaHCO_3$ (160 mg, 1.91 mmol) was added, after which extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 9 : 1) gave 4-*tert*-butyl-7-methoxy-2-(2-thienyl)-2*H*-azepine (**14**) (65 mg, Y = 52%) as a colorless oil and 5-*tert*-butyl-2-methoxy-3-(2-thienyl)-3*H*-azepine (**16**) (6 mg, Y = 5%) as a colorless oil.

4-*tert*-butyl-7-methoxy-2-(2-thienyl)-2*H*-azepine (**14**)

1H NMR (500 MHz, $CDCl_3$) δ 1.15 (s, 9H), 3.77 (s, 3H), 4.21 (brs, 1H), 5.81 (d, $J = 5.5$ Hz, 1H), 6.56 (d, $J = 12.0$ Hz, 1H), 7.01-7.05 (m, 3H), 7.23 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.8 (q), 34.8 (s), 53.9 (q), 55.5 (d), 122.4 (d), 123.6 (d), 124.7 (d), 126.8 (d), 129.5 (d), 139.0 (d), 147.4 (s), 154.4 (s), 161.5 (s); IR (neat) 2968, 1634, 1444, 1247, 1205, 696 cm^{-1} ; UV-vis (EtOH) λ_{max} 234 nm (log $\epsilon = 3.82$), 286 nm (log $\epsilon = 3.38$); MS (FAB) m/z 262 $[M + H]^+$.

5-*tert*-butyl-2-methoxy-3-(2-thienyl)-3*H*-azepine (**16**)

1H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 9H), 3.45 (brs, 1H), 3.72 (s, 3H), 5.33 (d, $J = 6.0$ Hz, 1H), 6.23 (d, $J = 8.7$ Hz, 1H), 6.97- 7.04 (m, 3H), 7.27 (dd, $J = 5.0, 1.2$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1 (q), 34.8 (s), 44.5 (d), 55.2 (q), 115.1 (d), 115.3 (d), 124.4 (d), 125.9 (d), 126.4 (d), 136.9 (d), 140.7 (s), 147.3 (s), 152.5 (s); IR (neat) 2966, 1620, 1319, 1280, 1249, 1011, 696 cm^{-1} ; UV-vis (EtOH) λ_{max} 239 nm (log $\epsilon = 4.10$), 256 nm (log $\epsilon = 3.74$); MS (FAB) m/z 262 $[M + H]^+$.

Reaction of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (1) with thiophene in the presence of FeCl₃

A solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**) (100 mg, 0.478 mmol), thiophene (3.1 ml, 40 mmol), and iron trichloride (8 mg, 0.05 mmol) in chloroform (30 ml) was refluxed for 24 hours, after which water was added. The solution was extracted with chloroform. The extract was dried over MgSO₄ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 9 : 1) gave 5-*tert*-butyl-2-methoxy-7-(2-thienyl)-3*H*-azepine (**15**) (18 mg, Y = 14%) as a colorless oil and 5-*tert*-butyl-2-methoxy-3-(2-thienyl)-3*H*-azepine (**16**) (3 mg, Y = 2%) as a colorless oil.

5-*tert*-butyl-2-methoxy-7-(2-thienyl)-3*H*-azepine (15)

¹H NMR (500 MHz, CDCl₃) δ 1.15 (s, 9H), 2.67 (brs, 2H), 3.82 (s, 3H), 5.22 (t, *J* = 7.0 Hz, 1H), 6.73 (s, 1H), 7.03 (dd, *J* = 5.0, 3.5 Hz, 1H), 7.21 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.33 (dd, *J* = 3.5, 1.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 30.3, 32.7, 35.1, 54.7, 109.2, 110.0, 122.1, 124.7, 127.5, 141.6, 146.5, 148.7, 154.5; IR (neat) 2966, 1634, 1441, 1328, 1259, 1191, 1035, 826, 698 cm⁻¹; UV-vis (EtOH) λ_{max} 245 nm (log ε = 3.87), 310 nm (log ε = 4.16); MS (FAB) *m/z* 262 [M + H]⁺.

Reaction of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (1) with furan in the presence of FeCl₃

A solution of 4-*tert*-butyl-2,7-di-methoxy-2*H*-azepine (**1**) (300 mg, 1.43 mmol), furan (1.0 ml, 13 mmol), and iron trichloride (23 mg, 0.14 mmol) in chloroform (30 ml) was refluxed for 24 hours, after which water was added. The solution was extracted with chloroform. The extract was dried over MgSO₄ and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 9 : 1) gave 5-*tert*-butyl-7-(2-furyl)-2-methoxy-3*H*-azepine (**18**) (40 mg, Y = 11%) as a colorless oil and 5-*tert*-butyl-3-(2-furyl)-2-methoxy-3*H*-azepine (**19**) (7 mg, Y = 2%) as a colorless oil.

5-*tert*-butyl-7-(2-furyl)-2-methoxy-3*H*-azepine (18)

^1H NMR (300 MHz, CDCl_3) δ 1.17 (s, 9H), 2.68 (d, $J = 6.9$ Hz, 2H), 3.82 (s, 3H), 5.24 (t, $J = 6.9$ Hz, 1H), 6.43 (dd, $J = 3.3, 1.8$ Hz, 1H), 6.58 (d, $J = 3.3$ Hz, 1H), 6.84 (s, 1H), 7.42 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.2 (q), 32.7 (t), 35.1 (s), 54.6 (q), 106.6 (d), 109.6 (d), 109.7 (d), 111.4 (d), 138.3 (s), 141.8 (d), 148.8 (s), 154.5 (s), 155.7 (s); IR (neat) 2966, 1634, 1330, 1263, 1183, 1023, 1006, 808, 731 cm^{-1} ; UV-vis (EtOH) λ_{max} 234 nm (sh, $\log \epsilon = 3.90$), 297 nm ($\log \epsilon = 4.21$); MS (FAB) m/z 246 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 246.1494, found 246.1502.

5-*tert*-butyl-3-(2-furyl)-2-methoxy-3*H*-azepine (19)

^1H NMR (300 MHz, CDCl_3) δ 1.15 (s, 9H), 3.23 (d, $J = 6.6$ Hz, 1H), 3.70 (s, 3H), 5.39 (dd, $J = 6.6, 0.9$ Hz, 1H), 6.24 (dd, $J = 8.7, 0.9$ Hz, 1H), 6.29 (d, $J = 3.3$ Hz, 1H), 6.41 (dd, $J = 3.3, 1.8$ Hz, 1H), 7.02 (d, $J = 8.7$ Hz, 1H), 7.46 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.1 (q), 34.8 (s), 43.0 (d), 55.2 (q), 107.1 (d), 110.2 (d), 112.0 (d), 115.2 (d), 136.9 (d), 141.9 (d), 147.7 (s), 151.3 (s), 152.5 (s); IR (neat) 2968, 1622, 1319, 1286, 1251, 1228, 1013, 733 cm^{-1} ; UV-vis (EtOH) λ_{max} 250 nm ($\log \epsilon = 3.69$); MS (FAB) m/z 246 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 246.1494, found 246.1480.

Reaction of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (1) with pyrrole in the presence of FeCl_3

A solution of 4-*tert*-butyl-2,7-dimethoxy-2*H*-azepine (**1**) (100 mg, 0.478 mmol), pyrrole (0.50 ml, 7.2 mmol), and iron trichloride (8 mg, 0.05 mmol) in chloroform (30 ml) was stirred for 24 hours at room temperature, after which water was added. The solution was extracted with chloroform. The extract was dried over MgSO_4 and evaporated *in vacuo*. Chromatographic treatment of the residue on silica gel (hexane : ethyl acetate = 9 : 1) gave 5-*tert*-butyl-2-methoxy-7-(2-pyrrolyl)-3*H*-azepine (**21**) (13 mg, Y = 11%) as a colorless oil, 5-*tert*-butyl-2-methoxy-3-(2-pyrrolyl)-3*H*-azepine (**22**) (14 mg, Y = 12%) as colorless prisms and 2-[5-*tert*-butyl-2-methoxy-2*H*-pyrrol-2-yl-(*E*)-vinyl]pyrrole (**24**) (43 mg, Y = 37%) as colorless

prisms.

5-*tert*-butyl-2-methoxy-7-(2-pyrrolyl)-3*H*-azepine (21)

^1H NMR (300 MHz, CDCl_3) δ 1.15 (s, 9H), 2.67 (d, $J = 6.6$ Hz, 2H), 3.81 (s, 3H), 5.13 (t, $J = 6.6$ Hz, 1H), 6.26 (ddd, $J = 3.6, 2.7, 2.7$ Hz, 1H), 6.49 (ddd, $J = 3.6, 2.1, 1.5$ Hz, 1H), 6.63 (s, 1H), 6.78 (ddd, $J = 2.7, 2.7, 1.5$ Hz, 1H), 8.90 (brs, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.3 (q), 32.8 (t), 35.1 (s), 54.5 (q), 103.8 (d), 107.5 (d), 107.9 (d), 110.0 (d), 117.1 (d), 132.9 (s), 139.3 (s), 148.9 (s), 154.7 (s); IR (neat) 3450, 2966, 1632, 1535, 1460, 1439, 1334, 1265, 1183, 1096, 1035, 804, 719 cm^{-1} ; UV-vis (EtOH) λ_{max} 231 nm (sh, $\log \epsilon = 3.89$), 313 nm ($\log \epsilon = 4.24$); MS (FAB) m/z 245 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 245.1654, found 245.1631; Found: C, 73.59; H, 8.23; N, 11.73%. Calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$: C, 73.74; H, 8.25; N, 11.47%.

5-*tert*-butyl-2-methoxy-3-(2-pyrrolyl)-3*H*-azepine (22)

mp 129-130 $^{\circ}\text{C}$; ^1H NMR (200 MHz, CDCl_3) δ 1.12 (s, 9H), 3.17 (d, $J = 6.0$ Hz, 1H), 3.73 (s, 3H), 5.25 (d, $J = 6.0$ Hz, 1H), 6.13 (brm, 1H), 6.25 (d, $J = 8.6$ Hz, 1H), 6.22 (ddd, $J = 2.7, 2.7, 2.7$ Hz, 1H), 6.83 (ddd, $J = 2.7, 2.7, 1.5$ Hz, 1H), 7.02 (d, $J = 8.6$ Hz, 1H), 8.48 (brs, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ 30.0 (q), 34.6 (s), 42.6 (d), 55.1 (q), 107.3 (d), 108.1 (d), 114.7 (d), 115.3 (d), 117.7 (d), 128.3 (s), 136.9 (d), 147.2 (s), 152.7 (s); IR (KBr) 3222, 2962, 1599, 1325, 1243, 1009, 791, 712 cm^{-1} ; UV-vis (EtOH) λ_{max} 250 (sh) nm ($\log \epsilon = 3.68$); MS (FAB) m/z 245 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 245.1654, found 245.1621; Found: C, 73.90; H, 8.32; N, 11.38%. Calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$: C, 73.74; H, 8.25; N, 11.47%.

2-[5-*tert*-butyl-2-methoxy-2*H*-pyrrol-2-yl-(*E*)-vinyl]pyrrole (24)

mp 116.5-117.5 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 0.98 (s, 9H), 3.95 (s, 3H), 6.06 (d, $J = 5.0$ Hz, 1H), 6.15-6.17 (m, 2H), 6.21 (d, $J = 16.0$ Hz, 1H), 6.37 (d, $J = 16.0$ Hz, 1H), 6.72 (ddd, $J = 2.1, 2.1, 2.1$ Hz, 1H), 7.34 (d, $J = 5.0$ Hz, 1H), 8.22 (brs, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ 26.4 (q), 37.5 (s), 55.1 (q), 85.4 (s), 107.8 (d), 109.5 (d), 118.2 (d), 120.0 (d), 121.6 (d), 122.9 (d), 130.5 (s),

156.6 (d), 171.1 (s); IR (KBr) 3300, 2970, 1625, 1549, 1448, 1379, 1282, 777, 719 cm^{-1} ; UV-vis (EtOH) λ_{max} 289 nm ($\log \epsilon = 4.10$); MS (FAB) m/z 245 $[\text{M} + \text{H}]^+$; HRMS (FAB) m/z calcd for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 245.1654, found 245.1646; Found: C, 73.79; H, 8.18; N, 11.72%. Calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$: C, 73.74; H, 8.25; N, 11.47%.

Heating a CHCl_3 solution of **5**

The solution of 4-*tert*-butyl-7-methoxy-2-phenyl-2*H*-azepine (**5**) (30 mg, 0.118 mmol) in CHCl_3 (30 ml) was stirred for 24 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-2-methoxy-7-phenyl-3*H*-azepine (**11**) (30 mg, Y = 100%) as a colorless oil.

5-*tert*-butyl-2-methoxy-7-phenyl-3*H*-azepine (**11**)

^1H NMR (500 MHz, CDCl_3) δ 1.15 (s, 9H), 2.64 (brs, 2H), 3.83 (s, 3H), 5.25 (t, $J = 7.0$ Hz, 1H), 6.72 (s, 1H), 7.26 (t, $J = 7.5$ Hz, 1H), 7.38 (dd, $J = 7.5, 7.5$ Hz, 2H), 7.80 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 30.2 (q), 32.6 (t), 35.0 (s), 54.5 (q), 109.4 (d), 111.8 (d), 126.0 (d), 127.5 (d), 128.2 (d), 140.9 (s), 146.5 (s), 149.1 (s), 153.4 (s); IR (neat) 2966, 1636, 1328, 1259, 1180, 766, 694 cm^{-1} ; UV-vis (EtOH) λ_{max} 228 nm ($\log \epsilon = 4.00$), 288 nm ($\log \epsilon = 3.98$); MS (FAB) m/z 256 $[\text{M} + \text{H}]^+$; Found: C, 79.61; H, 8.30; N, 5.17%. Calcd for $\text{C}_{17}\text{H}_{21}\text{NO}$: C, 79.96; H, 8.29; N, 5.49%.

Heating a CHCl_3 solution of **7a**

The solution of 4-*tert*-butyl-7-methoxy-2-(4-methoxyphenyl)-2*H*-azepine (**7a**) (50 mg, 0.175 mmol) in CHCl_3 (30 ml) was stirred for 24 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-2-methoxy-7-(4-methoxyphenyl)-3*H*-azepine (**12a**) (50 mg, Y = 100%) as colorless prisms.

5-*tert*-butyl-2-methoxy-7-(4-methoxyphenyl)-3*H*-azepine (**12a**)

mp 104.5-105.5 °C; ^1H NMR (500 MHz, CDCl_3) δ 1.15 (s, 9H), 2.63 (brs, 2H), 3.82 (s, 3H), 3.83

(s, 3H), 5.22 (t, $J = 6.5$ Hz, 1H), 6.64 (s, 1H), 6.91 (d, $J = 9.0$ Hz, 2H), 7.73 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 30.2 (q), 32.6 (t), 35.0 (s), 54.4 (q), 55.3 (q), 108.7 (d), 110.3 (d), 113.6 (d), 127.1 (d), 133.7 (s), 146.2 (s), 149.2 (s), 153.3 (s), 159.3 (s); IR (KBr) 2966, 1638, 1607, 1508, 1323, 1249, 1178, 1036, 830 cm^{-1} ; UV-vis (EtOH) λ_{max} 221 nm ($\log \epsilon = 3.50$), 290 nm ($\log \epsilon = 3.75$); MS (FAB) m/z 286 $[\text{M} + \text{H}]^+$; Found: C, 75.70; H, 8.06; N, 5.05%. Calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_2$: C, 75.76; H, 8.12; N, 4.91%.

Heating a CHCl_3 solution of **7b**

The solution of 4-*tert*-butyl-7-methoxy-2-(2-methoxyphenyl)-2*H*-azepine (**7b**) (50 mg, 0.175 mmol) in CHCl_3 (30 ml) was stirred for 96 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-2-methoxy-7-(2-methoxyphenyl)-3*H*-azepine (**12b**) (50 mg, Y = 100%) as a colorless oil.

5-*tert*-butyl-2-methoxy-7-(2-methoxyphenyl)-3*H*-azepine (**12b**)

^1H NMR (300 MHz, CDCl_3) δ 1.18 (s, 9H), 2.71 (d, $J = 7.5$ Hz, 2H), 3.78 (s, 3H), 3.85 (s, 3H), 5.25 (t, $J = 7.5$ Hz, 1H), 6.80 (s, 1H), 6.95 (d, $J = 7.5$ Hz, 1H), 7.00 (ddd, $J = 7.5, 7.5, 1.2$ Hz, 1H), 7.27 (ddd, $J = 7.5, 7.5, 1.8$ Hz, 1H), 7.63 (dd, $J = 7.5, 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.2 (q), 32.5 (t), 34.9 (s), 54.4 (q), 55.8 (q), 109.4 (d), 111.7 (d), 116.2 (d), 120.4 (d), 128.3 (d), 129.9 (d), 130.8 (s), 144.2 (s), 148.8 (s), 153.5 (s), 156.6 (s); IR (neat) 2954, 1630, 1323, 1213, 1180, 1023, 752 cm^{-1} ; UV-vis (EtOH) λ_{max} 283 nm ($\log \epsilon = 3.98$); MS (FAB) m/z 286 $[\text{M} + \text{H}]^+$.

Heating a CHCl_3 solution of **9a**

The solution of 4-*tert*-butyl-2-(4-hydroxyphenyl)-7-methoxy-2*H*-azepine (**9a**) (30 mg, 0.111 mmol) in CHCl_3 (30 ml) was stirred for 24 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-7-(4-hydroxyphenyl)-2-methoxy-3*H*-azepine (**13a**) (30 mg, Y = 100%) as colorless prisms.

5-*tert*-butyl-7-(4-hydroxyphenyl)-2-methoxy-3*H*-azepine (13a)

mp 113.0-114.0 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.16 (s, 9H), 2.62 (brs, 2H), 3.82 (s, 3H), 4.85 (brs, 1H), 5.22 (t, *J* = 6.9 Hz, 1H), 6.63 (s, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 30.3 (q), 32.7 (t), 35.1 (s), 54.5 (q), 108.8 (d), 110.3 (d), 114.9 (d), 127.3 (d), 133.7 (s), 146.0 (s), 149.0 (s), 153.3 (s), 155.1 (s); IR (KBr) 3380, 2952, 1638, 1611, 1510, 1441, 1334, 1261, 1180, 1023, 832 cm⁻¹; UV-vis (EtOH) λ_{max} 243 nm (log ε = 3.92), 293 nm (log ε = 4.24); MS (FAB) *m/z* 272 [M + H]⁺; HRMS (FAB) *m/z* calcd for C₁₇H₂₂NO₂ [M + H]⁺ 272.1651, found 272.1610; Found: C, 75.04; H, 7.73; N, 5.21%. Calcd for C₁₇H₂₁NO₂: C, 75.25; H, 7.80; N, 5.16%.

Heating a CHCl₃ solution of 9b

The solution of 4-*tert*-butyl-2-(2-hydroxyphenyl)-7-methoxy-2*H*-azepine (**9b**) (30 mg, 0.111 mmol) in CHCl₃ (30 ml) was stirred for 24 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-7-(2-hydroxyphenyl)-2-methoxy-3*H*-azepine (**13b**) (30 mg, Y = 100%) as colorless prisms.

5-*tert*-butyl-7-(2-hydroxyphenyl)-2-methoxy-3*H*-azepine (13b)

mp 124.0-125.0 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.14 (s, 9H), 2.60 (brs, 2H), 3.82 (s, 3H), 5.26 (t, *J* = 7.0 Hz, 1H), 6.59 (s, 1H), 6.86 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 6.91 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.20 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 7.33 (dd, *J* = 7.5, 1.5 Hz, 1H), 11.7 (s, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 30.1 (q), 32.3 (t), 35.1 (s), 55.1 (q), 109.4 (d), 114.4 (d), 117.0 (d), 119.4 (d), 124.4 (s), 127.4 (d), 129.2 (d), 146.2 (s), 149.9 (s), 154.7 (s), 156.0 (s); IR (KBr) 3080, 2952, 1638, 1607, 1446, 1336, 1272, 1245, 752 cm⁻¹; UV-vis (EtOH) λ_{max} 278 nm (log ε = 3.89), 314 nm (log ε = 3.93); MS (FAB) *m/z* 272 [M + H]⁺; Found: C, 75.24; H, 8.04; N, 5.13%. Calcd for C₁₇H₂₁NO₂: C, 75.25; H, 7.80; N, 5.16%.

Heating a CHCl₃ solution of **95**

The solution of 4-*tert*-butyl-7-methoxy-2-(2-thienyl)-2*H*-azepine (**14**) (30 mg, 0.115 mmol) in CHCl₃ (30 ml) was stirred for 24 hours at 50°C. Evaporation of the solution gave 5-*tert*-butyl-2-methoxy-7-(2-thienyl)-3*H*-azepine (**15**) (30 mg, Y = 100%) as a colorless oil.

5-*tert*-butyl-2-methoxy-7-(2-thienyl)-3*H*-azepine (**15**)

¹H NMR (500 MHz, CDCl₃) δ 1.15 (s, 9H), 2.67 (brs, 2H), 3.82 (s, 3H), 5.22 (t, *J* = 7.0 Hz, 1H), 6.73 (s, 1H), 7.03 (dd, *J* = 5.0, 3.5 Hz, 1H), 7.21 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.33 (dd, *J* = 3.5, 1.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 30.3 (q), 32.7 (t), 35.1 (s), 54.7 (q), 109.2 (d), 110.0 (d), 122.1 (d), 124.7 (d), 127.5 (d), 141.6 (s), 146.5 (s), 148.7 (s), 154.5 (s); IR (neat) 2966, 1634, 1441, 1328, 1259, 1191, 1035, 826, 698 cm⁻¹; UV-vis (EtOH) λ_{max} 245 nm (log ε = 3.87), 310 nm (log ε = 4.16); MS (FAB) *m/z* 262 [M + H]⁺.

3. Supplementary explanation

3-1. The half life of **14**

Measuring the decrease in intensity of the peaks attributed to azepine ring-protons in ¹H NMR spectrum is a convenient way to estimate the rate of 1,5-H shift of **14**. The reaction was able to analyze as first order reaction, because the plot of ln *a/a*₀ versus *t* shows a liner correlation on 62°C (Figure 2, Table 3). We are planning to report the detailed study of the thermal 1,5 shift in 2*H*-azepine.

Figure 2. Plot of $\ln(a/a_0)$ versus t for the determination of rate constant k at 62°C for the 1,5-H shift of **14** in CDCl_3 .

Table 3. Rate constant k and half life for 1,5-H shift of **14** to **15** in CDCl_3 at 62°C

T / °C	k / min ⁻¹	$t_{1/2}$ / min	r^a
62	1.71×10^{-2}	40.6	0.9999

^a r is the respective linear correlation coefficient.

3-2. The discussion about of the reaction of 2-methoxy-2*H*-azepine with FeCl_3 .

The increase in the amounts of FeCl_3 caused the ring-opening reaction of 2-methoxy-2*H*-azepine **1** to produce **25** and **26** (Scheme 4). The structure of **25** was determined by NMR, IR, and MS spectrum. The signals of δ_{H} 9.69 (d, $J = 7.5$ Hz, 1H) and δ_{C} 193.1 (d) suggests that an aldehyde is present in the structure of **25**. The doublet signal of the aldehyde in ^1H NMR spectrum shows the spin-spin coupling for the adjacent olefinic proton [δ_{H} 6.05 (dd, $J = 7.5, 1.5$ Hz, 1H)]. The signals of δ_{H} 6.23 (d, $J = 12.5$ Hz, 1H) and δ_{H} 6.74 (dd, $J = 12.5, 1.5$ Hz, 1H) suggests the *Z*-ethylene structure based on $^3J_{\text{HH}}$ value. In the IR spectrum, two signals of 1734 and 1676 cm^{-1} for carbonyl absorption were observed. The absorption of 1734 cm^{-1} is attributed to ester. The absorption of

1676 cm^{-1} is attributed to $\alpha,\beta,\gamma,\delta$ -unsaturated aldehyde; a typical absorption of $\alpha,\beta,\gamma,\delta$ -unsaturated aldehyde has been known as 1680-1660 cm^{-1} .¹⁸ Methyl 4-*t*-butyl-6-oxo-hexa-2*Z*,4*E*-dienoate (**25**) was gradually isomerized to more stable 2*E*,4*E*-isomer **26** in CDCl_3 at room temperature (Scheme 5). The structure of **26** was characterized by the value of $^3J_{\text{HH}} = 15.8 \text{ Hz}$ for *E*-ethylene moiety.

Scheme 4. A plausible mechanism for the ring-opening reaction of **1** with FeCl_3

Scheme 5. Thermal isomerization of **25** to **26**

^aAM1 calculated heat of formation

methyl 4-*tert*-butyl-6-oxo-hexa-2*Z*,4*E*-dienoate (**25**)

25 is known compound (ref. 5).

^1H NMR (500 MHz, CDCl_3) δ 1.19 (s, 9H), 3.66 (s, 3H), 6.05 (dd, $J = 7.5, 1.5 \text{ Hz}$, 1H), 6.23 (d, $J = 12.5 \text{ Hz}$, 1H), 6.74 (dd, $J = 12.5, 1.5 \text{ Hz}$, 1H), 9.69 (d, $J = 7.5 \text{ Hz}$, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ 28.8 (q), 37.5 (s), 51.5 (q), 125.1 (d), 125.4 (d), 139.1 (d), 165.0 (s), 168.0 (s), 193.1 (d); IR (neat) 2974, 1734, 1676, 1437, 1228, 1180, 1151, 826 cm^{-1} ; UV-vis (EtOH) λ_{max} 236 nm (log ϵ

= 4.02); MS (FAB) m/z 197 $[M + H]^+$.

methyl 4-*tert*-butyl-6-oxo-hexa-2E,4E-dienoate (26)

^1H NMR (200 MHz, CDCl_3) δ 1.17 (s, 9H), 3.81 (s, 3H), 6.01 (d, $J = 15.8$ Hz, 1H), 6.13 (d, $J = 7.8$ Hz, 1H), 7.49 (d, $J = 15.8$ Hz, 1H), 9.72 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ 28.7 (q), 36.8 (s), 51.8 (q), 127.4 (d), 127.7 (d), 139.9 (d), 165.2 (s), 168.3 (s), 192.4 (d); IR (neat) 2956, 1729, 1682, 1632, 1437, 1274, 1174, 1147 cm^{-1} ; MS (FAB) m/z 197 $[M + H]^+$.

A plausible mechanism for the formation of **9b** is shown in Scheme 6.

Scheme 6. A plausible mechanism for the formation of **9b**

A plausible mechanism for the formation of **20** and **22** is shown Scheme 7.

Scheme 7. A plausible mechanism for the formation of **20** and **22**

The significant difference between the products formed in the reactions with TiCl_4 and FeCl_3 may be attributed to the difference in the affinities of O and N atoms in **1** for Lewis acids (Scheme 8). It is considered that mainly O atom of **1** coordinates to TiCl_4 . On the other hand, it is considered that both O and N atoms of **1** can coordinate to FeCl_3 .

Scheme 8. A plausible difference in the affinities of O and N atoms in **1** for Lewis acids